8EHQ-1102-15225

DuPont Haskell Laboratory
for Health and Environmental Sciences
Elkton Road, P.O. Box 50
Newark, DE 19714-0050

November 25, 2002

Via Federal Express

Document Processing Center (Mail Code 7407M)
Room 6428
Attention 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency, ICC Building
1201 Constitution Ave., NW
Washington, D.C. 20460

Contain NO CBI

Dear 8(e) Coordinator:

4,4'-Oxydianiline
[CAS # 101-80-4]

This letter is to inform you of the results of a recently completed rat pilot developmental toxicity study with the above referenced test substance.

Groups of 8 time-mated Crl:CD®(SD)IGS BR rats were dosed once daily by gavage at dose levels of 0, 6.25, 12.5, 25 or 50 mg/kg/day over days 6-20 of gestation (day 6-20G). The vehicle was polyethylene glycol (PEG 400) and the dose volume was 4 ml/kg/day. During the in-life portion of the study, maternal body weights, food consumption, and clinical signs data were collected. On day 21G, all dams were euthanized and examined grossly. Gravid and empty uterine weights were recorded to permit calculation of the adjusted maternal final body weight. The uterine contents were examined and described; (number and status of implantation sites, and fetal assessment – viable, nonviable, location, sex, fetal weight, external alterations).

There was no test substance-related maternal mortality nor were there any test substance-related maternal gross postmortem findings. Clinical observations were limited to persistent localized alopecia at 25 and 50 mg/kg/day. Maternal toxicity was observed at all dose levels and included statistically significant, test substance-related reductions in maternal body weights, weight changes and food consumption.

At the 50 mg/kg/day dose level, two animals had implantation sites but no fetuses, indicating very early resorption of their litters. The mean number of late resorptions per litter was increased at 25 and 50 mg/kg/day (0.3 and 0.6, respectively vs. 0.0 in the control group); although not statistically significant at 25 mg/kg/day, this finding was considered possibly test substance-related. There was a statistically significant reduction in mean pup weight at 50 mg/kg/day (72% of control mean). Test substance-related external malformations consisting of anasarca and cleft palate (1 and 7 affected fetuses, respectively, in 1 of 5 litters examined) were observed at 50 mg/kg/day. No other test substance-related external alterations were observed at any dose level. Sex ratio and litter size were comparable across all groups.

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In a 90-day feeding and one-generation reproduction study previously conducted in rats, the number of pups per litter at birth was decreased at 400 ppm in the presence of decreased maternal body weights, body weight gains and food efficiency. This dietary level corresponded to an average daily intake of 31 mg/kg/day for female rats. Thus, the developmental/reproductive toxicity that was observed in the 90-day feeding/one-generation reproduction study and the pilot developmental study occurred at similar dose levels, i.e. 31 and 25 mg/kg/day, respectively.

The main developmental toxicity study is currently in progress.

Under these experimental conditions, the findings described above appear to be reportable, based upon guidance given in the EPA TSCA Section 8(e) Reporting Guide (June, 1991).

Sincerely,

A. Michael Kaplan

A. Michael Kaplan, Ph.D.
Director – Regulatory Affairs and Occupational Health

AMK/EM:clp
(302) 366-5260

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